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Advances in High Sensitivity Microcoil NMR

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High Sensitivity NMR Program Plan

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- **Portable LC-NMR system development**
  - Non-destructive, no added reagents, structure and isotope specific, quantitative field deployable analysis system
  - Field analysis of signatures of
    - Nuclear reprocessing analytes
    - HE and HE degradation products
    - Chemical agents

- **High resolution, high sensitivity LC-NMR (lab based)**
  - Improved analysis in lab of signatures
    - Library development, degradation pathways, etc.
  - Analysis of mass limited samples
  - Molecular “tag” and antibody development for BW agents

- **Micron-scale chemical-selective imaging**
  - Elasticity and porosity of composite materials
  - Cellular structure, cellular chemistry, cellular interactions

Reducing the size of the NMR coil significantly increases NMR sensitivity

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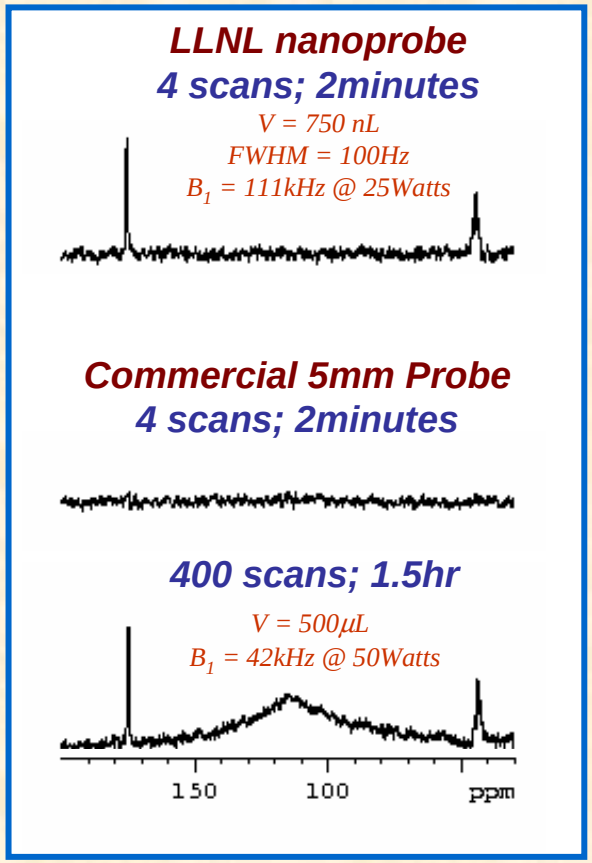
RF Coil – dual purpose:

- Delivers radiofrequency pulses to sample
- Detects precessing magnetization to ultimately produce NMR spectrum
- Sensitivity ~ S/N per mole
- Signal S(t)

$$S(t) = NV\omega_0 M_{xy}(t) B_{xy}$$

where

$$B_{xy} = \frac{n\mu_0}{d_{coil}\sqrt{1+\left(\ell_{coil}/d_{coil}\right)^2}}$$



High resolution NMR spectra of ^{13}C-Glycine
(15 mg diluted to 750 nL for nanoprobe and 500μL for commercial probe)

70x sensitivity enhancement

We are using advanced lithography methods to design and construct new NMR microcoils

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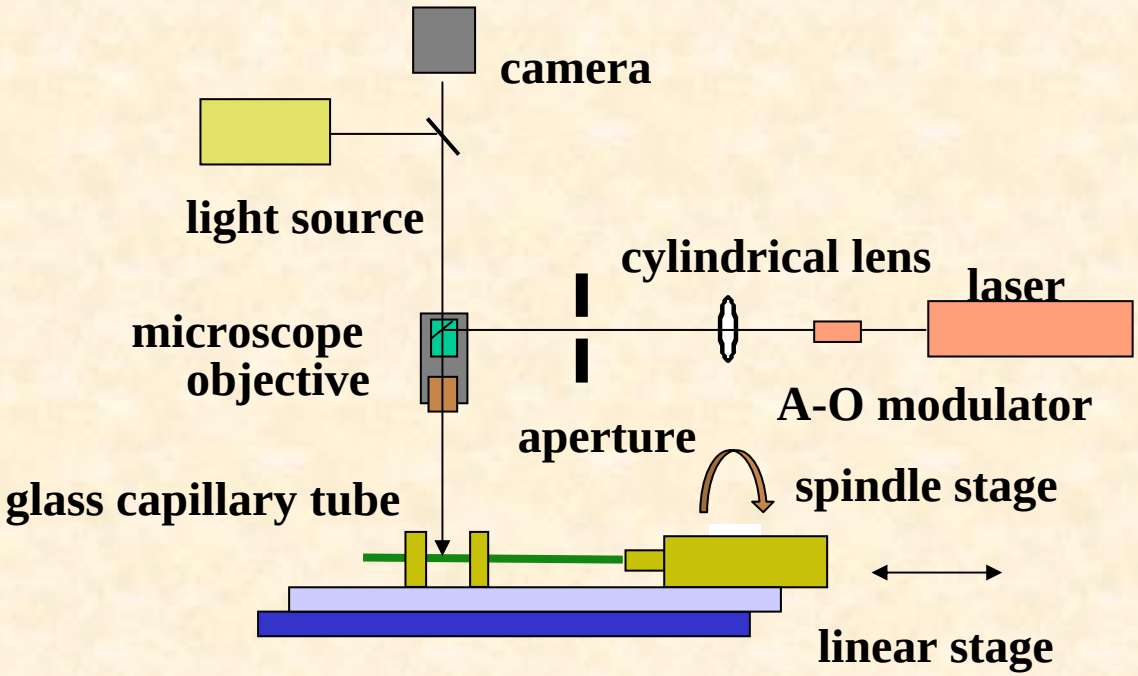
Laser direct-write system consisting of a focused Ar-ion laser and a spindle stage for rotation and a linear stage for translation of the target.



LLNL Laser Lithography (L-Lathe) Process

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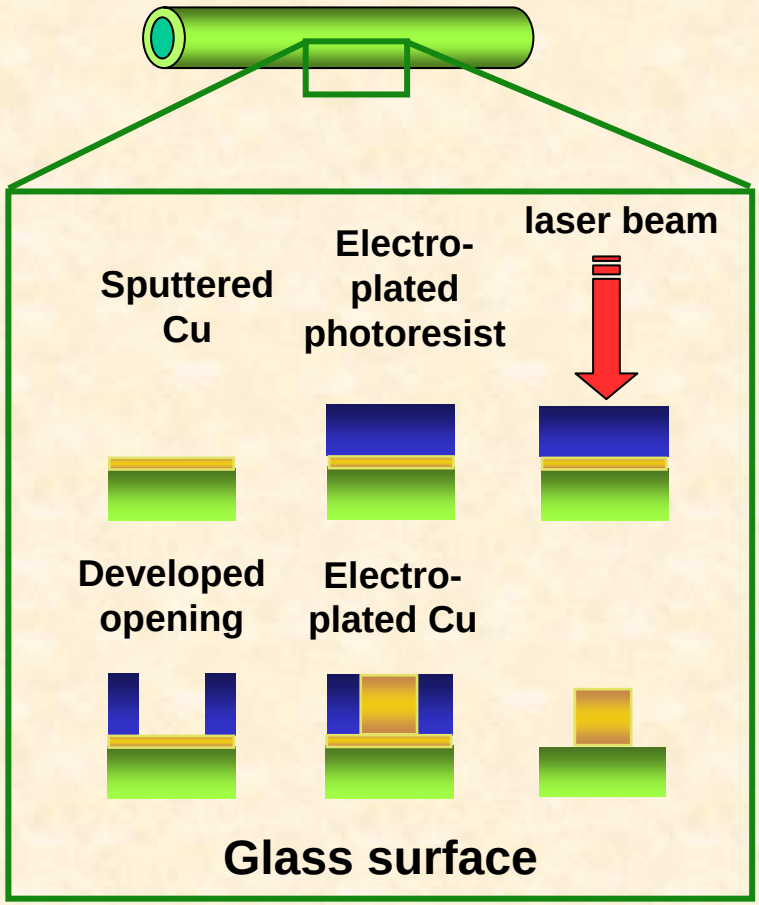

- Capillary surface is coated with a seed layer of Cu.
- The seed layer is then coated with a positive electrodeposited photoresist.
- The photoresist is exposed by the L-lathe system in the pattern of the desired coil form.
- Copper is electroplated through the resist mask to form the RF coil.
- Residual photoresist is removed, leaving Cu coil form.

Development of Microcoils with Lithography

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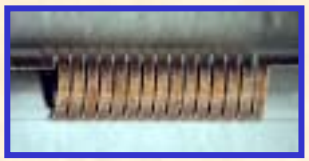
Smaller Diameter



1 mm o.d.

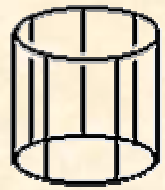
360 µm o.d.

Different Shapes

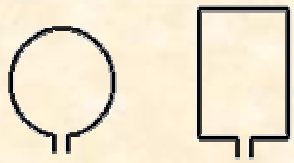
solenoid

Birdcage coil

- Generate MR pickup, shim, and gradient coils of various designs to ≥100 µm
- Direct incorporation of LC separation and flow stages
- Direct incorporation of multiplex methods
- **Microcoils also will allow us to overcome the largest hurdle to success of a portable system: resolution!**
  - **Smaller coils require less homogenous B_0**
  - **Fabrication methodology uniquely suited for construction of coils for field compensation and specific sample geometries**
  - **Incorporation of CAD allows custom coils to be built precisely to specifications**



Bird Cage Coil



Surface Coils

Paired Saddle Coil

Helmholtz Pair Coil

High Sensitivity Portable LC-NMR

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Concept:

- **Develop technology to construct**
  - High field (>2T)
  - Compact (potentially hand held)
  - Field deployable NMR instrument
  - Parallel and/or serial with other portable analytical equipment
- **System will be based on NMR microcoils developed at LLNL which offer**
  - Improved sensitivity
  - Decreased size (coil and magnet)
  - Decreased power requirements

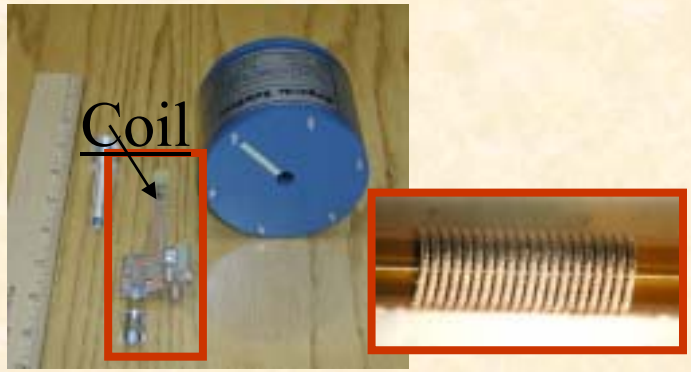
Result:

- **A compact, field deployable unit that can stand alone or be added in series or parallel with other portable analytical tools.**

The Competition:

- **< 0.5T**
- **~2 briefcases**
- **No LC-NMR capabilities**

Varian 900 MHz NMR Spectrometer (21.1 Tesla)



NMR Probe and Initial Results

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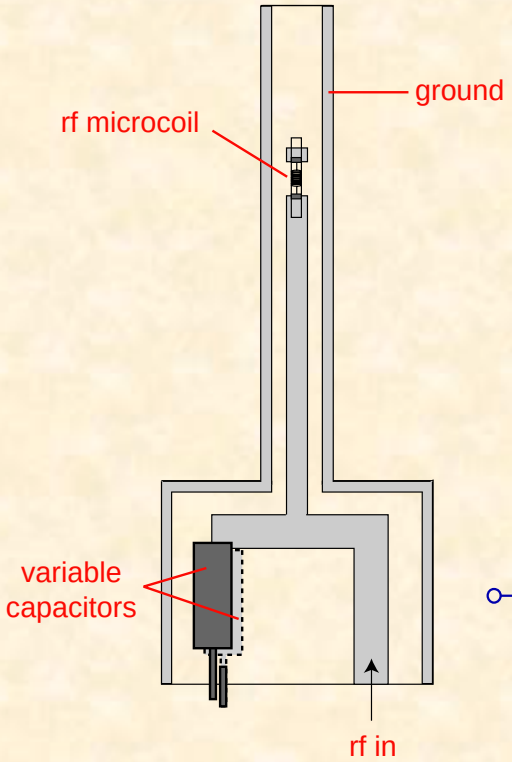
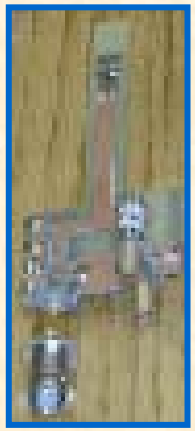
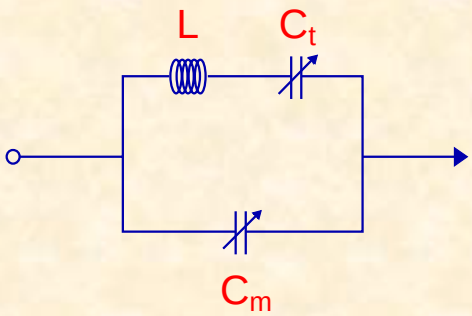
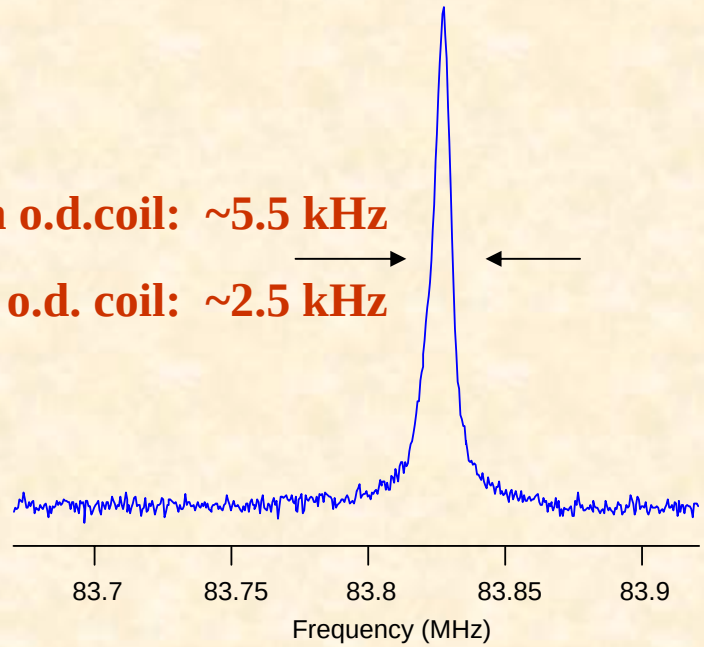






1 mm o.d.coil: ~5.5 kHz

360 μm o.d. coil: ~2.5 kHz



NMR probe: LC tank circuit on circuit board

^{1}H spectrum of H_2O in 2T magnet

Ultimate linewidth goals: ⊙ 100Hz

Resolution enhancements are necessary.

Portable LC-NMR: Current and Future Work

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Resolution enhancement

- Modeling and design of shim coils
- Fabrication of shim coils using laser lithography

Shim coil modeling and construction

LC system

- Design of miniature transmission line flow probe
- Incorporation of separation and flow stages
- Start with lab-based system, work towards miniaturization

NMR console

- Compact RF generation
- Data acquisition system

High Sensitivity LC-NMR for Analysis of Nuclear Proliferation

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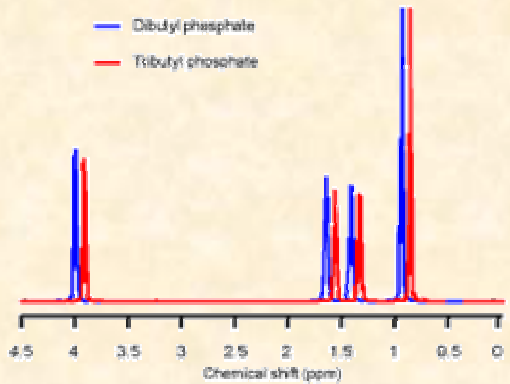
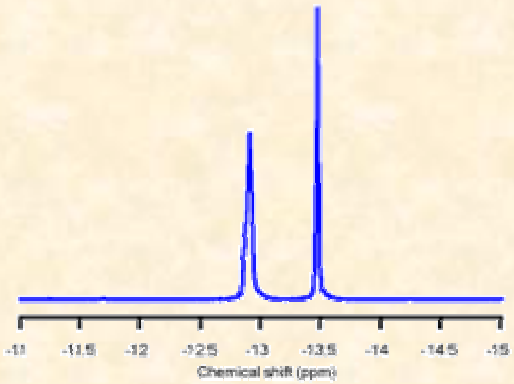
- NMR can determine presence of individual or combinations of chemical signatures indicative of nuclear and chemical proliferation.
- Use of a commercial NMR spectrometer allows us to develop the necessary hardware used for the integration of the LC system.
  - Double resonance (^{1}H and ^{31}P) transmission line flow probe designed and built.
- Use of the lab based system is allowing us to test newly developed microcoils, as well as examine environmentally relevant mock F&T scenarios.

A field deployable unit that combines LC and multiplex microcoil NMR will be used to obtain and validate structural specific NP signatures.

^{1}H NMR of dibutyl phosphate and tributyl phosphate



^{31}P NMR of dibutyl phosphate/ tributyl phosphate mixture



NMR is a versatile screening tool for chemical weapon signatures

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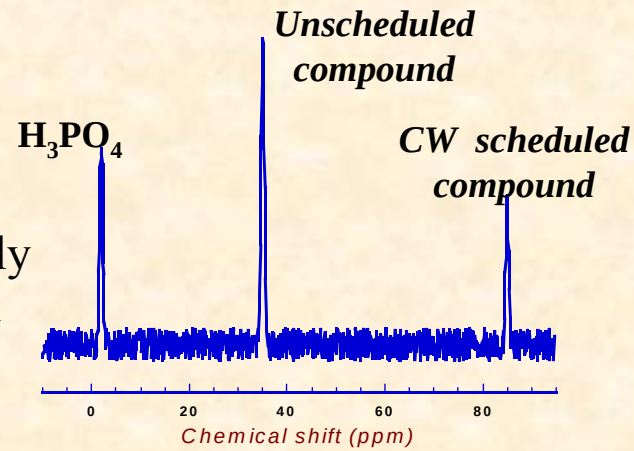
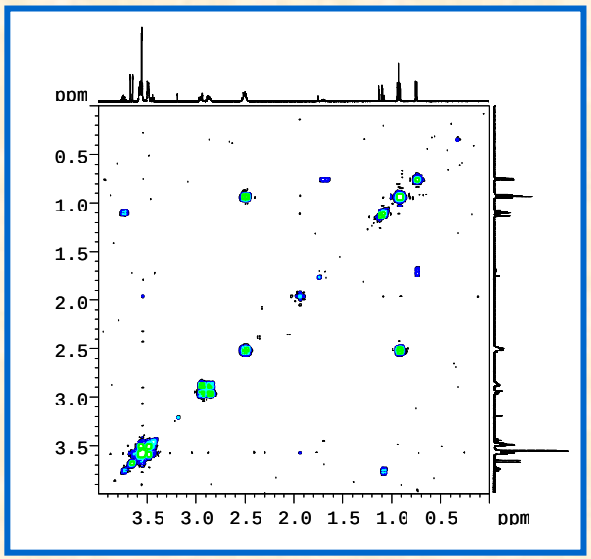
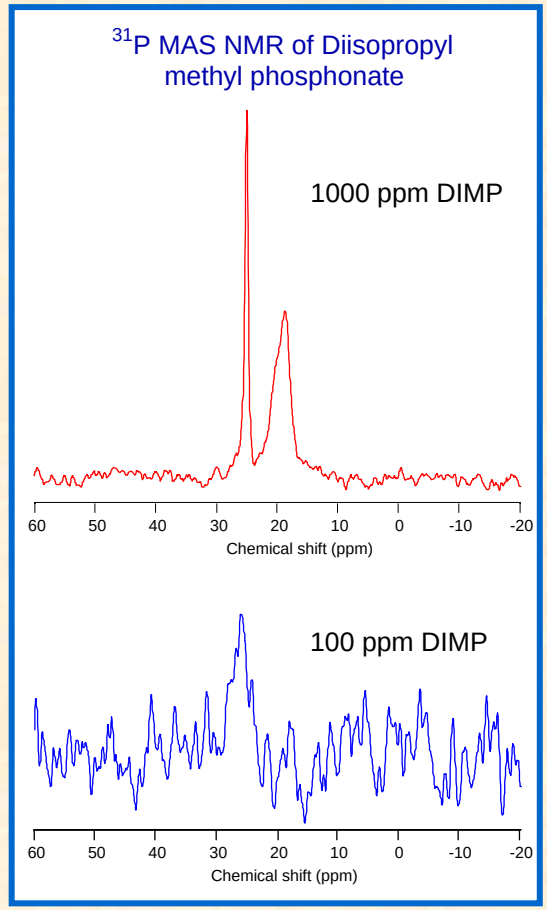
NMR is a required OPCW screening method:

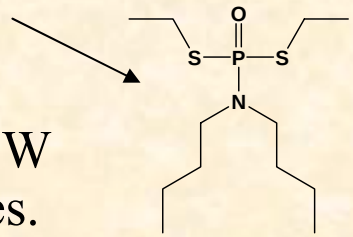
- Organo-phosphates distinguished unambiguously on the basis of ^{31}P chemical shift.





Portable NMR instrument will enable field detection of small concentration of CW agents.





NMR can detect and structurally characterize CW agents in complex mixtures.

Future Applications of Microcoil NMR and Microimaging

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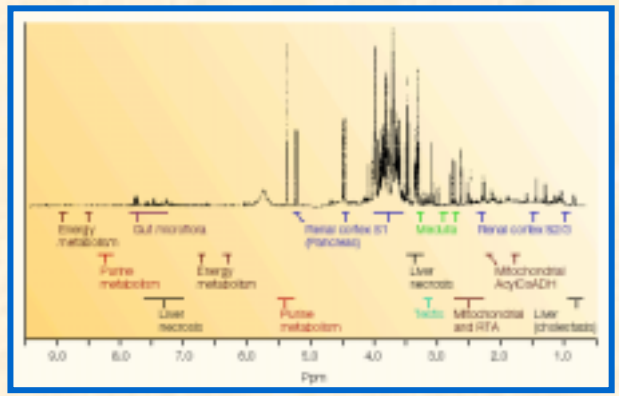
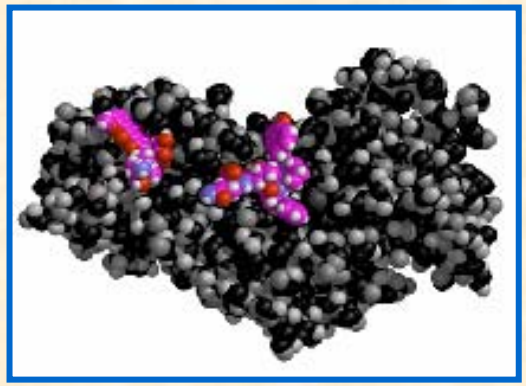
- **Metabonomics**
  - High sensitivity metabolite recognition in biofluids will provide presymptomatic detection of drugs or disease.

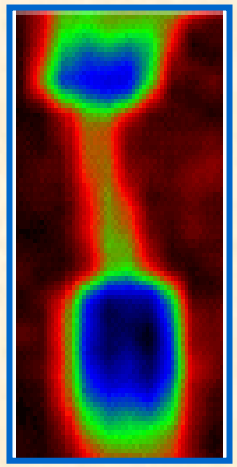


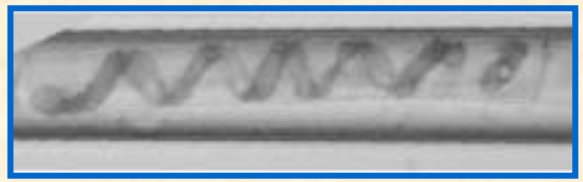
Nature Reviews, **1**, 153 (2002)

- **Rapid screening for High Affinity Ligands**
  - Identification of unique binding sites will aid in the design of new molecules such as synthetic antibodies.

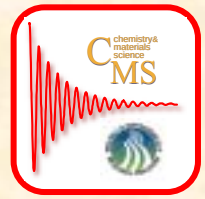


- **Three dimensional imaging**
  - Cellular imaging
  - ICF/HED targets
  - Optically pumped xenon and microcoils to give detailed 3D images





Acknowledgements



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Portable NMR system

Hardware design, microcoil development, shim coil design

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Vince Malba

OPCW

Robert Maxwell
Hugh Gregg
Armando Alcaraz

Fate & transport

John Reynolds
Lee Davisson
Carolyn Koester
August Droege

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BSNL
LDRD

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High affinity ligands

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Felice Lightstone
Christine Hartmann-Siantar

Cellular microimaging

Julie Herberg
Krish Krishnan
Michael Thelen
Rod Balhorn